UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/688,246	10/16/2003	Chenera Balan	A-825	2469

21069 7590 02/24/2006

AMGEN INC.
MAIL STOP 28-2-C
ONE AMGEN CENTER DRIVE
THOUSAND OAKS, CA 91320-1799

EXAMINER	
BERNHARDT, EMILY B	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 02/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/688,246	BALAN ET AL.	
	Examiner	Art Unit	
	Emily Bernhardt	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/16/03 & 3/26/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicants' election of Group II and in particular species of eg.8 without traverse is acknowledged. However in view of the differing issues of patentability that exists for subject matter within elected Group II as evidenced at the very least by art of record such as WO'271 which is relevant to R4 as pyrrolidine or US 6,197,772 which teaches R4 as piperidines or US'028 which teaches in addition to piperidines, azepines as well as pyrrolidines as R4 as well as the many differing permutations permitted at R4 as well as "Q" ring system which do not share common classification but rather cover classes such as 540 and 544 and many various subclasses, the subject matter of Group II has been narrowed to a specific type of R4 ring as well as the "Q" ring system which can be benzo or aza-containing with up to 4 N atoms. Thus, based on elected species of eg.8 subject matter within II that will be examined consists of R4= pyridine or dihydro or tetrahydro derivatives optionally substituted as set forth in the claims but not further fused with Q3-Q6 being all C atoms. All of the pending claims read in part on the elected subject matter. Applicants are advised that the claims will only be examined with respect to this subject matter.

The abstract of the disclosure is objected to because it does depict structural makeup of claimed subject matter by way of a formula. Correction is required. See MPEP § 608.01(b).

Claims 1 and 3-10 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for species in claim 11, does not reasonably provide enablement for entire scope of substituents permitted on benzimidazole,piperazine and pyridine rings. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The scope alone at benzimidazole ring system is huge since substitution is permitted at every ring position and includes heterocyclic rings having as many as 4 hetero atoms in any array with further fusion thereon and having any degree of unsaturation. Starting material sources for such rings are not seen in the specification nor reaction conditions needed to prepare mono- to persubstituted benzimidazoles,piperazines and/or pyridines. Note In re Howarth 210 USPQ 689 and Ex parte Moersch 104 USPQ 122 for the need to show starting materials commensurate with the instant scope. There is no reasonable basis for assuming that the myriad of compounds embraced by the all the generic claims will all share the physiological properties needed to practice the invention since they are so structurally dissimilar as to being chemically non-equivalent and there is no basis in the prior art for assuming the same. The same applies for the scope of remaining substituents permitted on these rings which includes sulfides, many different types

of sulfonyl groups, amidines,ureas, guanidines,etc. Compounds made are predominately substituted on the benzimidazole ring with halo or CF_3 and to a lesser extent with simple amino,carboxy-derived groups,sulfonamide, cyano, nitro. Some exemplify at the 7-position monocyclic heteroaryls, namely pyrazine, pyridine,pyrimidyl,thienyl,furyl and pyrrolyl as well as saturated azines-morpholino, piperazino, piperidino. No more than disubstitution is exemplified. Piperazine rings is mainly unsubstituted with a few examples of lower alkyl or alkoxy. Pyridine (or hydrogenated analog) is mainly substituted with CF_3 or halo at the 3-position with fewer examples of carboxamido,COOH, CH_2OH, allylic alcohol or N-acylated groups. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art.

Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition, which includes factors such as:

1) Breadth of the claims- the claims cover compounds easily in the billions as pointed out above;

2) Level of unpredictability in the art- the invention is pharmaceutical in nature as it involves binding to vanilloid receptors. It is well established that "the

scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be unpredictable. See In re Fisher 166 USPQ 18. Clearly the functional groups permitted herein vary not only considerably in their size (surface area) but also in polarity and electronic effects- all factors for consideration in selecting compounds for receptor binding;

3) Direction or guidance- as stated above the compounds made are not representative of the instant scope but represent a small fraction;

4) State of the prior art- The compounds are piperazine derivatives with benzimidazole at one end and a pyridine ring (or di- or tetrahydro derivative thereof) with a multitude of substitution permitted at all ring positions. While such compounds are known as evident from the art applied below, they are similar in structure to the compounds made herein and thus do not evidence the many structural permutations permitted in the instant scope are known activity relied on herein;

5) Working examples- No test data has been presented only mention that (unidentified) compounds have been tested and thus no clear evaluation of which functional groups at various positions out of the many claimed might affect potency to a large or small degree.

In view of the above considerations, this rejection is being applied.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1,3,4 and 7-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Sun (US'111 A1). Sun is applied as of its earliest US provisional filing date of 12/24/02 since anticipated subject matter is described therein. Sun describes many compounds within the instant scope when instant R4 is pyridyl. See Table VI beginning on p.159-160, Table VIII, p.166-168, Table X on p.173-174, Table XII on p.180-181. Said compounds are taught for uses based on activity as antagonists for glutamate receptors (mGluR1 and mGluR5) and as ligands for the VR1 receptor.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5-6 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sun. The teachings of Sun as discussed in the above 102 rejection is incorporated herein. Compounds in 5 and 6 require that a substituent be present at either the 4- or 7- position in addition to the requirement in claim 1 that one of Q4 or Q5 must be substituted. Thus compounds such as CAW or CBS on p.159 of Sun are adjacent position isomers of compounds covered by these claims. Position isomers are not deemed patentably distinct absent evidence of superior,unexpected results. See In re Crounse 150 USPQ 554; Ex parte Engelhardt 208 USPQ 343 regarding position isomerism. While claim 11 lists many species that may not be particularly taught by Sun there are also obvious variants present including 5,6 disubstituted species such as the 5^{th},8^{th} or 11^{th} entries on p.14. These compounds differ from compounds in Sun, CCE, CCF,CCU in Table VI only in being disubstituted at the 5- and 6- positions vs monosubstitution in Sun's examples. However Sun teaches substitution at both ring positions as can be seen in the R8 and R9 definitions appearing on p.8. Thus it would have been obvious to one skilled in the art at the time the invention was made to expect instant 7- (or 4-) substituted derivatives to also possess the uses taught by the applied art in view of their close structural similarity as well as 5,6 disubstituted derivatives in view of the equivalency

teachings outlined above.

It is recognized that applicants are claiming benefit of a US provisional case that has an earlier filing date than Sun's effective filing date but benefit is denied for the following reasons. To obtain such benefit there must be compliance with 35 USC 112, par.one - description and enablement. Claims rejected herein are not entirely described in provisional case. At the very least the scope of substituents permitted in R^c is far broader than what is disclosed in said priority papers. Also scope at R^5,$R^{5'}$,R^e does not appear to be coextensive with that claimed herein and R^h is not seen in the provisional application. Additionally,many of the species in claim 11 are not described therein as well. Also, the generic claims are not in compliance with 35 USC 112, first paragraph as outlined in the above rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

E Bernhardt

Emily Bernhardt
Primary Examiner
Art Unit 1624